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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/524,716 | 02/16/2006 | Masato Kato | 18655 | 8342 |

23389 7590 09/09/2010
SCULLY SCOTT MURPHY & PRESSER, PC
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| EXAMINER | |
|---|---|
| JUEDES, AMY E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 09/09/2010 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/524,716 | KATO ET AL. | |
| | Examiner | Art Unit | |
| | AMY E. JUEDES | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *11-13,15,19 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13,15,19 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/6/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's amendment and remarks, filed 7/6/10, are acknowledged. Claims 11-13, 15, 19, and 23 are pending and are being acted upon.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-13, 15, 19, and 23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/24078, in view of U.S. Patent 5,316,920 (of record), as evidenced by U.S. Patent 5,766,570 (of record).

WO 99/24048 teaches treating graft versus host disease (i.e. a method of down regulating the immunoactivity of a graft or treating a condition characterized by the inappropriate immunoactivity of a graft) by administering the antibodies that deplete dendritic cells to a subject (see page 20 and 22 in particular). WO 99/24078 teaches that the dendritic cells may be depleted using an antibody immunotoxin that binds to dendritic cell markers (see page 10-11 in particular). Additionally, WO 99/24078 teaches that the method results in the killing of the dendritic cells (i.e. cell lysis, see page 3 and 10, in particular). WO 99/24078 also teaches monoclonal antibodies (see page 12 in particular). WO 99/24078 also teaches that the antibodies can be administered concurrent with allogenic bone marrow transplantation (i.e. the administration of the antibodies results in the "contact" of the bone marrow graft with the antibodies in the subject, see page 20 in particular).

WO 99/24078 does not teach an antibody specific for CD83.

The '920 patent teaches a monoclonal antibody reactive with HB15 (i.e. CD83, see column 2 of the '570 patent which discloses that HB15 is another name for CD83, and see column 3, 5, and 10 of the '920 patent, in particular). The '920 patent teaches that HB15 is expressed by dendritic cells (see column 5 and 10, in particular). The '920 patent teaches that the antibodies can be used therapeutically to deliver toxins to HB15 expressing cells (i.e. to induce cell lysis, see column 3, first full paragraph, in particular). The '920 patent teaches that the antibodies can be used as therapeutic agents to treat human organ transplants and to inhibit an immune response (see columns 2-3 and 13, in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to perform the therapeutic method of treating graft versus host disease by administering an antibody specific for an antigen presenting dendritic cell, as taught by WO 99/24078, using the HB15 antibody taught by the '920 patent. The ordinary artisan would have been motivated to do so, and have a reasonable expectation of

success, since WO 99/24078 teaches that antibody depletion of dendritic cells is useful for treating graft versus host disease, and the '920 patent teaches that HB15 is an antigen expressed by dendritic cells, and that the antibody can be used to deliver toxins (i.e. an immunotoxin) to said cells.

Applicant's arguments filed 7/6/10 have been fully considered, but they are not persuasive.

Applicant argues that the ordinary artisan would not have expected antibodies that target CD83 to be useful in the methods now claimed, due to the unpredictably nature of antibody therapy. Applicant particularly notes that the WO 99/24078 reference itself teaches that not all dendritic cell antibodies eliminate dendritic cells in vivo, as shown in example 2.

WO 99/24078 teaches that in vivo treatment with a dendritic cell specific antibody results in the binding of the antibody to dendritic cells, but not the elimination of the dendritic cells. However, WO 99/24078 teaches that the experiment was only performed for proof of principle for the use of a toxin conjugated antibody (i.e. it is toxin that is meant to induce cell lysis in the method of WO 99/24078, not the antibody alone, see page 31, lines 20, in particular). Thus, while it might be unpredictable as to whether administration of a particular unconjugated antibody would result in depletion of bound cells, WO 99/24078 teaches that cell depletion can readily be achieved by linking antibodies to a toxin for inducing lysis of the bound cells. The ordinary artisan would have a reasonable expectation of success that any antibody that binds to a dendritic cell, when linked to a toxin, could be used to induce lysis of the bound dendritic cells, and Applicant has not provided any evidence to the contrary.

Applicant also argues that the immunological effects of dendritic cell antibodies can range from inhibition of maturation to enhanced immunopotentiation by preventing dendritic cell death, as taught by WO 01/02005 and U.S. Patent 7,052,694.

The examples cited by Applicant involve modulating the activity of dendritic cells by administering an unconjugated antibody. However, the method made obvious above does not involve modulating the activity of dendritic cells with a CD83 antibody, but rather makes obvious a method of depleting dendritic cells in vivo using a CD83 antibody conjugated to a toxic component (i.e. an immunotoxin). WO 99/24078 teaches

the feasibility of depleting dendritic cells with a toxin conjugated antibody specific to a wide range of dendritic cell specific markers, and that the antibody functions to direct the toxic component to the dendritic cells (see page 12, in particular). Even without knowing the function of CD83 (i.e. the effect of stimulating CD83 signaling with an antibody), the ordinary artisan would easily recognize that toxin conjugated CD83 antibodies would result in the delivery of the toxin to dendritic cells and the killing of said dendritic cells by the toxin. Thus, the method made obvious above does not require a particular function of CD83 as a lymphocyte activation molecule, but rather requires CD83 merely to act as a marker for targeting dendritic cells to which the toxin will be delivered. The '920 patent clearly discloses CD83 as a marker for dendritic cells. The ordinary artisan would have had a reasonable expectation that linking the CD83 antibody to a toxin (as taught by WO 99/24078 and the '920 patent) would induce lysis of CD83 expressing cells in vivo, thus "downregulating" the immuno-activities of the cells. Furthermore, the ordinary artisan would have a reasonable expectation that depleting dendritic cells would function to treat graft versus host disease, based on the teachings of WO 99/24078.

3. No claim is allowed.

4. **THIS ACTION IS MADE FINAL**. See Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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